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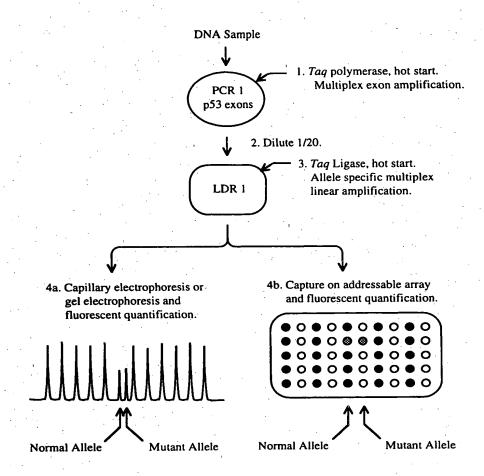
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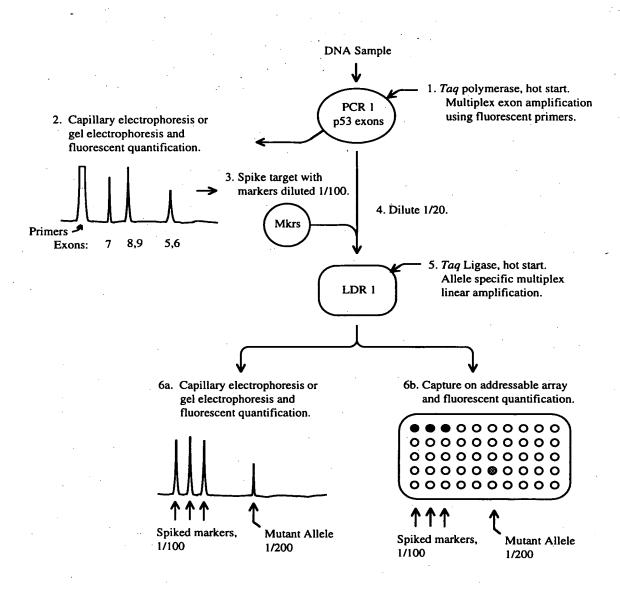
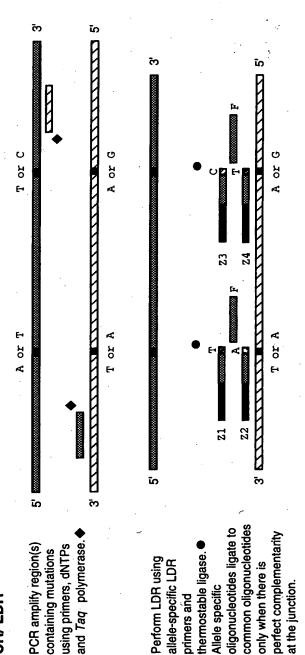


FIG. 2



## PCR/ LDR

using primers, dNTPs and Taq polymerase. 1. PCR amplify region(s) containing mutations



2. Perform LDR using allele-specific LDR

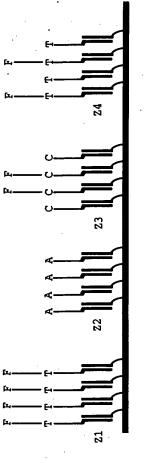
primers and

products on addressable array and quantify each 3. Capture fluorescent allele.

only when there is

Allele specific

at the junction.



Homozygous: T allele only.

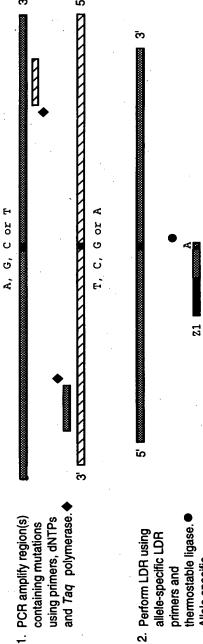
Heterozygous: C and T alleles.

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### PCR/ LDR

using primers, dNTPs and Taq polymerase. 1. PCR amplify region(s) containing mutations



T, C, G or A

3 Expression of the second sec

72

23

common oligonucleotides

perfect complementarity

at the junction.

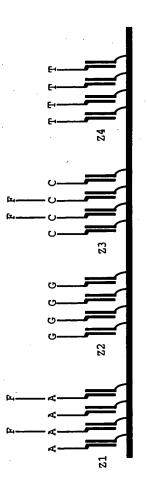
only when there is

oligonucleotides ligate to

Allele specific

primers and

22



products on addressable array and quantify each

allele.

3. Capture fluorescent

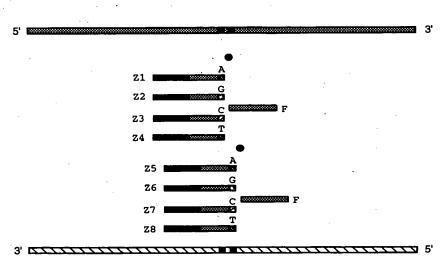
Heterozygous: A and C alleles.

#### PCR/LDR: N arby alleles

- PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase.
- A, G, C or T

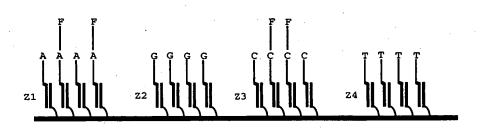
  5'

  T, C, G or A
- 2. Perform LDR using allele-specific LDR primers and thermostable ligase. Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.

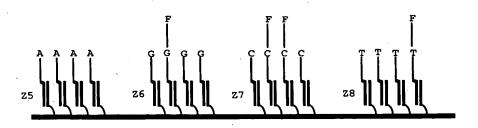


T, C, G or A

 Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: A and C alleles.



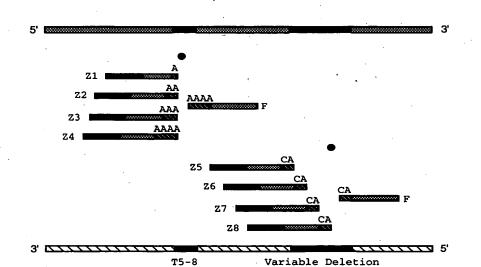
Heterozygous: G,C, and T alleles.

#### PCR/ LDR: Insertions and Deletions

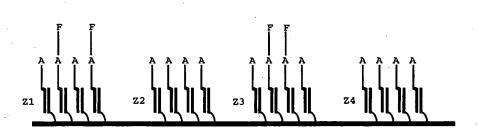
- PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase. ◆
- A5-8 Variable Deletion in (CA)n

  5'

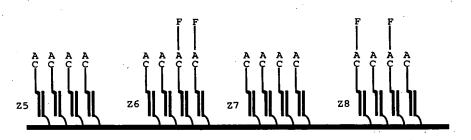
  T5-8 Variable Deletion in (GT)n
- 2. Perform LDR using allele-specific LDR primers and thermostable ligase. Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



 Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: A5 and A7 alleles.



Heterozygous: (CA)5 and (CA)3 alleles.



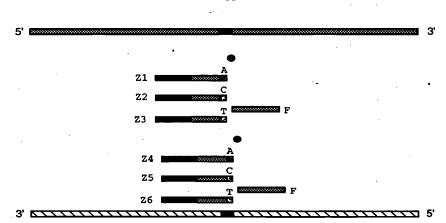


#### PCR/ LDR: Adjacent alleles, cancer detection

- PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase.
- Wildtype, GG

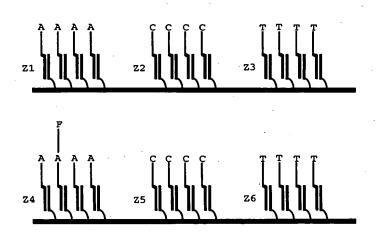
  5'

  Wildtype, CC
- 2. Perform LDR using allele-specific LDR primers and thermostable ligase. Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



Wildtype, CC

 Capture fluorescent products on addressable array and quantify each allele.



Gly to Asp mutation

#### PCR/ LDR: Nearby alleles

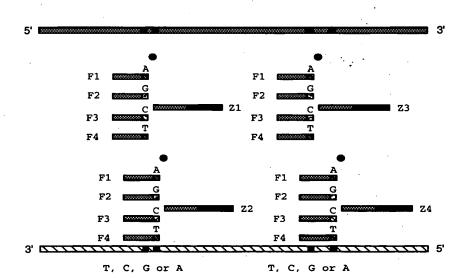
- PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase.
- A, G, C or T

  A, G, C or T

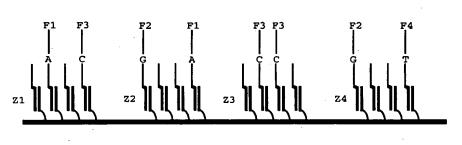
  5'

  T, C, G or A

  T, C, G or A
- 2. Perform LDR using allele-specific LDR primers and thermostable ligase. Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



 Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: A and C alleles.

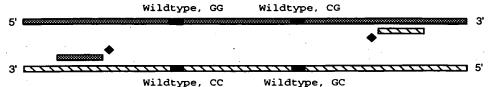
Heterozygous: A and G alleles.

Homozygous: C allele.

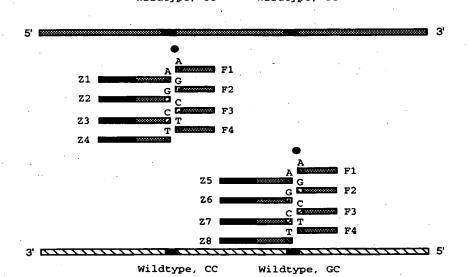
Heterozygous: G and T alleles.

#### PCR/ LDR: Adjacent and Nearby alleles

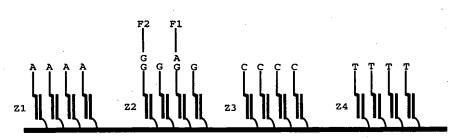
 PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase.



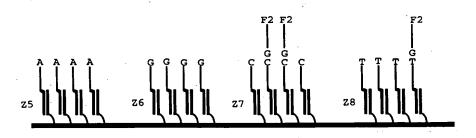
2. Perform LDR using allele-specific LDR primers and thermostable ligase. ● Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



 Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: Gly and Glu alleles.



Het rozygous: Arg and Trp alleles.



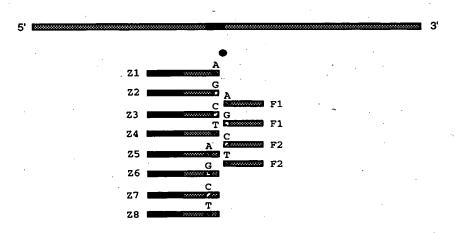
#### PCR/LDR: All all les of a single cod n

 PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase. Wildtype, CAA

5'

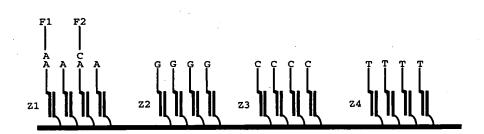
Wildtype, GTT

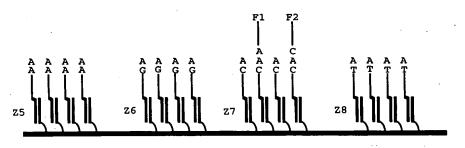
2. Perform LDR using allele-specific LDR primers and thermostable ligase. ● Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3' Wildtype, GTT

 Capture fluorescent products on addressable array and quantify each allele.





Heterozygous: Gln and His alleles.





```
X
                                                                       Y-PEG
                                                   (Y)-PEG-Y*
X,Y
                                         X^*, Y^* =
                                                            -O(C=O)Z
            -OH
                                                            -O(C=S)Z
             -CO<sub>2</sub>H
             –NH₂
                                                            -CO_2H
                                                            -(C=\bar{O})Z
(Y)
             W-NH-
                                                            -NH_2
                                                            -N=Č=O
W = protecting group, e.g. Boc, Fmoc
Z = activating group, e.g. imidazole (Im), p-nitrophenol (OPnp),
             hydroxysuccinimide (OSu), pentafluorophenol (OPfp)
PEG = oligo or poly(ethylene glycol), backbone (CH_2CH_2O)_n n = 6 to 200 (can also be grown by anionic polymerization with \frac{1}{C})
WSC = water soluble carbodiimide
Functional group transformations/activation (as needed), X \rightarrow X^*, Y \rightarrow Y^*
-OH \longrightarrow -O(CH_2)_nCO_2H  n = 1, 2
-OH \rightarrow -O(C=O)NHCH_2CO_2H
-OH \longrightarrow -O(C=O)CH_2NH_2
-OH \longrightarrow -O(C=O)Im
-OH \longrightarrow -O(C=S)SCH_2(C=O)NH_2
-CO_2H \rightarrow -(C=O)NH(CH_2)_nNH_2
                                            n = 2.6
-CO_2H \longrightarrow -(C=O)Z
-NH_2 \rightarrow -NH(C=O)(CH_2)_nCO_2H  n = 2, 3
Covalent linkage, X* + Y*
-CO_2H + H_2N - + WSC + HOSu \rightarrow -(C=O)NH
-OH + Im(\bar{C}=O)Im + H_2N - \longrightarrow -O(\bar{C}=O)NH
-OH + O=C=N- \rightarrow -O(C=O)NH-
-O(C=S)SCH_2(C=O)NH_2 + H_2N- \longrightarrow -O(C=S)NH-
                           + HO - \longrightarrow -OCH_2CH(OH)CH_2O-
-OH + ClCH<sub>2</sub>-
                          (+H<sub>2</sub>NH<sub>-</sub>)
```

#### FIG. 11

 $-OH \rightarrow -OCH_2(C=O)H + H_2N - + NaCNBH_3 \rightarrow -OCH_2CH_2NH -$ 



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FIG. 12B Ac-Cys-Probe + 
$$N-(CH_2)_nC-Support$$
 $n = 1, 2, \text{ or } 5$ 
 $pH 8$ 
 $CH_3C-N-CH-C-Probe$ 
 $CH_2$ 
 $CH_2$ 





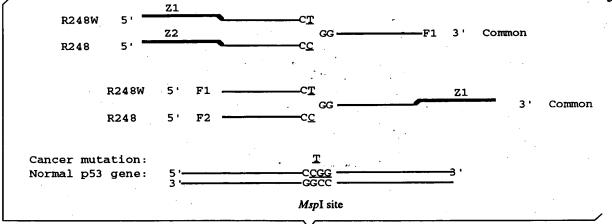
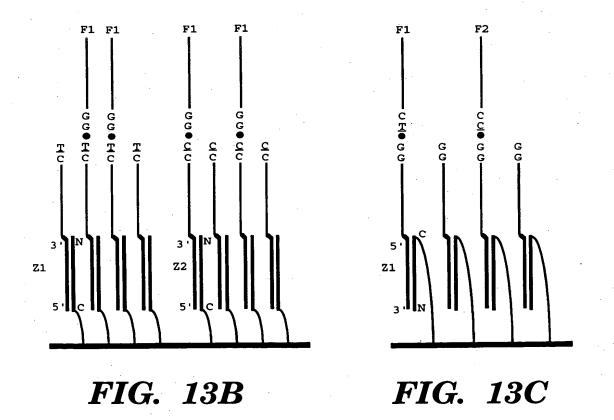


FIG. 13A





A B C D E F G H I J K L M N O

FIG. 14A

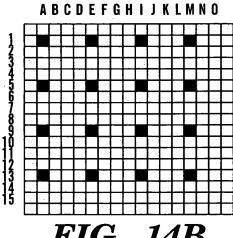
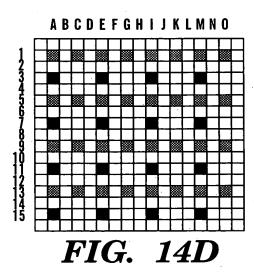


FIG. 14B



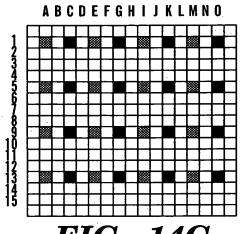
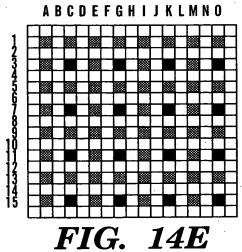


FIG. 14C



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FIG. 15A

1st addition of unique 24mers.

FIG. 15B

2nd addition of unique 24mers.

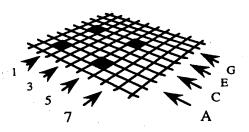
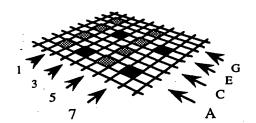


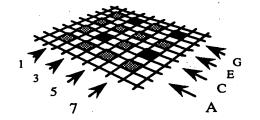
FIG. 15C
3rd addition of unique 24mers.

To the second se

FIG. 15D

4th addition of unique 24mers.





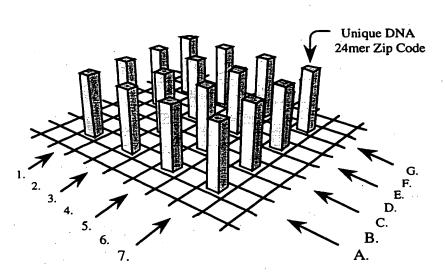


FIG. 15E



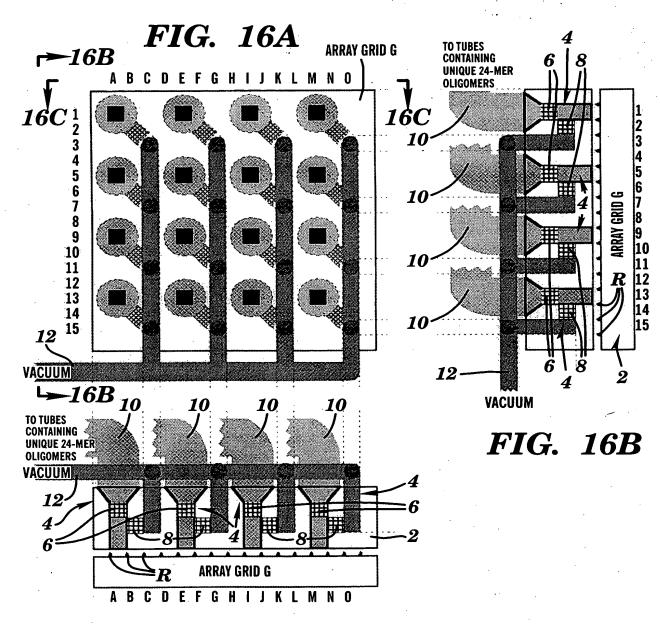


FIG. 16C



**2ND TWO** BASES 1ST TWO BASES GC GG GA AT AC AG AA TC TG TA CT CC CG CA GT TTGA TTAG 23' 6 8 16' TCTG 1 TCGT TCCC TC 6 30 TGAT 7 TGTC TGCG TG [11] 36' TACA 36 TA 33' 18' CTTG CTCA CTGT CT 8 32' 13 .11 CCAT 15 CCTA CC 29' CGAA CGTT CG 4' 28' 10 12 16 CAGC 12 CAGC CA 9' 34' 14 ĵij 25 GTGC GTCT GT 24' 31' 19 22 CGTT 17 GCAA GC 22' 14' 23 GGTA 18 GGAC GG 3' 20' 35' 24 GACC GATG 34 GAGT 21 GA 2' 20 ATAC ATCG AT 31 28 7 15 ACCT 27 ACGG AC 5' 29 13 ' 21' AGCC 35 AGGA AGTG 25 AG 27' 30 191 AAAG 32 AATC 26 AA 17' 10'

FIG. 17



1st Tetramer addition (columns)

1	2	3	4	5	
1	2	3	4	5	
1	2	3	4	5	
1	2	3	4	5	
1	2	3	4	5	

FIG. 18A

4th Tetramer addition (rows)

2	2	2	2	2
1	1	1	1	1
6	6	6	6	6
5	5	5	5	5
4	4	4 -	4	4

FIG. 18D

18/34

2nd Tetramer addition (rows)

6	6	6	6	6
5	5	5	5	. 5
4	. 4	4	4	4
3	3	3	3	3
2	2	2	2	2

FIG. 18B

5th Tetramer addition (columns)

6	1	2	3	4
6	1	2	3	4
6	1	2	3	4
6	1	2	3	4
6	1	2	3	4

FIG. 18E

3rd Tetramer addition (columns)

3	4	5	6	1
3	4	5	6	1
3	4	5	6	1
3	4	5	6	1
3	4	5	6	1

FIG. 18C

6th Tetramer addition (rows)

3	3	3	3	3
2	2	2	2	2
1	1	1	1	. 1
6	6	6	6	6
5.	5	5	5	5

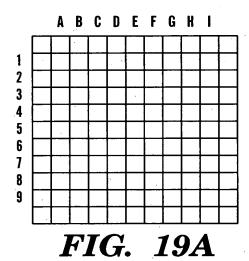
FIG. 18F

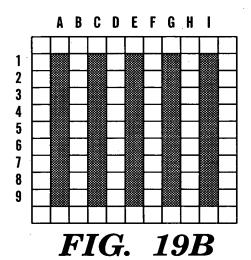
Addressable array with full length PNA 24mers

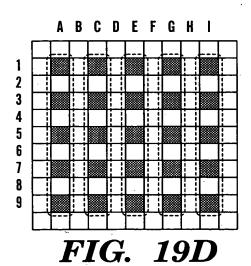
1-6-	3-2-6-3	2-6-4-2-1-3	3-6-5-2-2-3	4-6-6-2-3-3		5-6-1-2-4-3	
1-5-	3-1-6-2	2-5-4-1-1-2	3-5-5-1-2-2	4-5-6-1-3-2		5-5-1-1-4-2	
1-4-	3-6-6-1	2-4-4-6-1-1	3-4-5-6-2-1	<b>4-4-6-6-3-</b> 1	٠	5-4-1-6-4-1	
1-3-	3-5-6-6	2-3-4-5-1-6	3-3-5-5-2-6	4-3-6-5-3-6		5-3-1-5-4-6	
1-2-	-3-4-6-5	2-2-4-4-1-5	3-2-5-4-2-5	4-2-6-4-3-5		5-2-1-4-4-5	

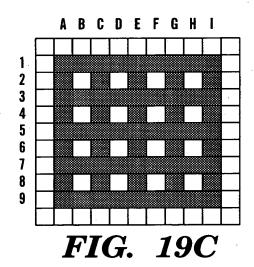
FIG. 18G











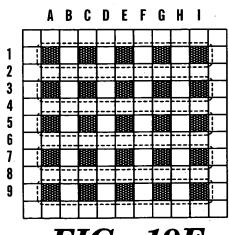


FIG. 19E

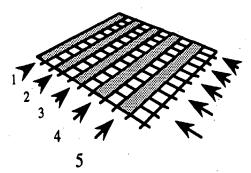


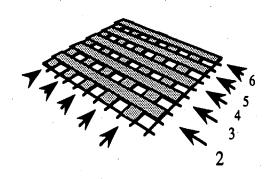
#### FIG. 20A

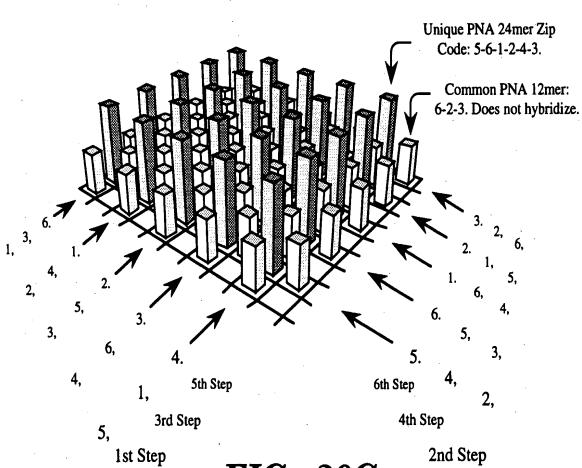
1st Tetramer additions (columns)

#### FIG. 20B

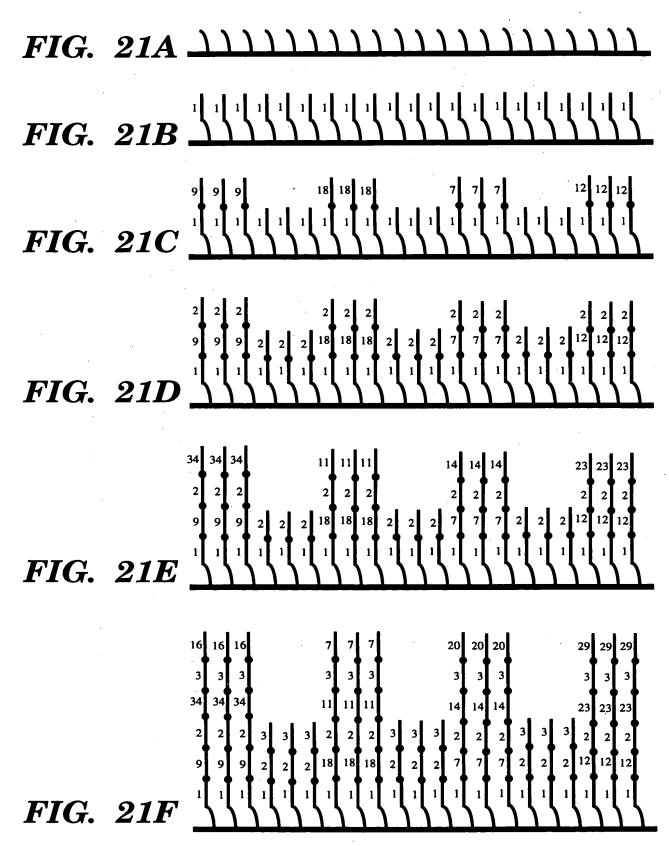
2nd Tetramer additions (rows)







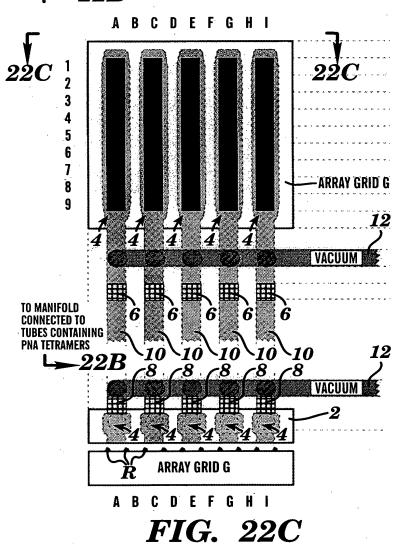






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TO MANIFOLD CONNECTED TO TUBES CONTAINING PNA TETRAMERS

2

FIG. 22B



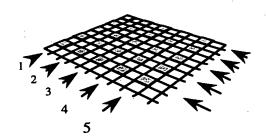
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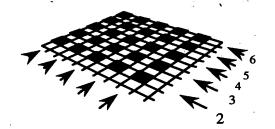
FIG. 23A

1st Tetramer additions (columns)

FIG. 23B

2nd Tetramer additions (rows)





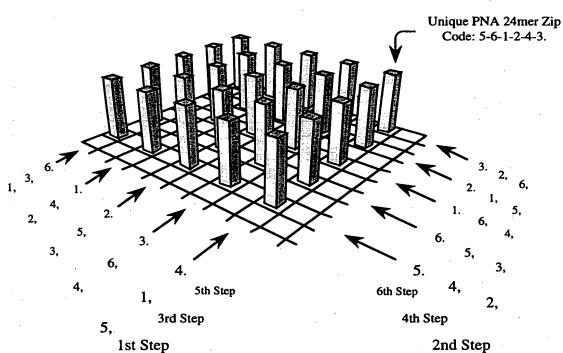


FIG. 23C

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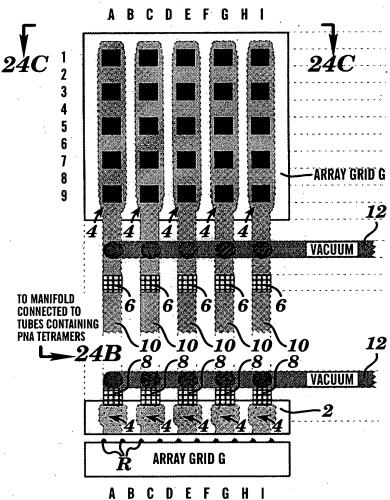
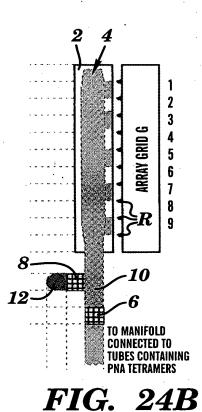
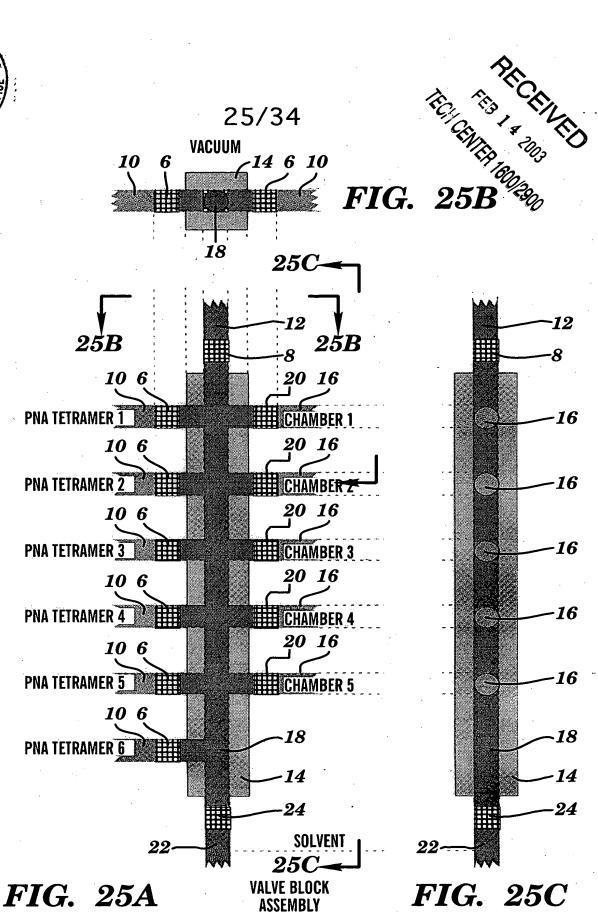


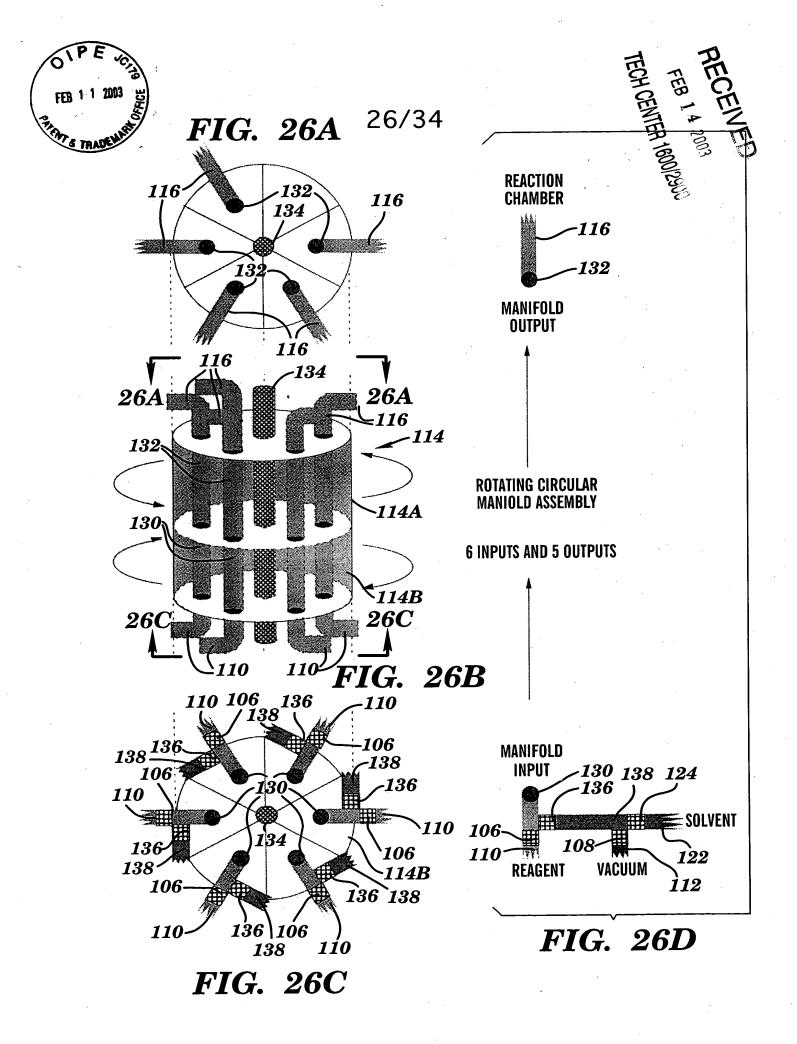
FIG. 24C







**6 INPUTS AND 5 OUTPUTS** 





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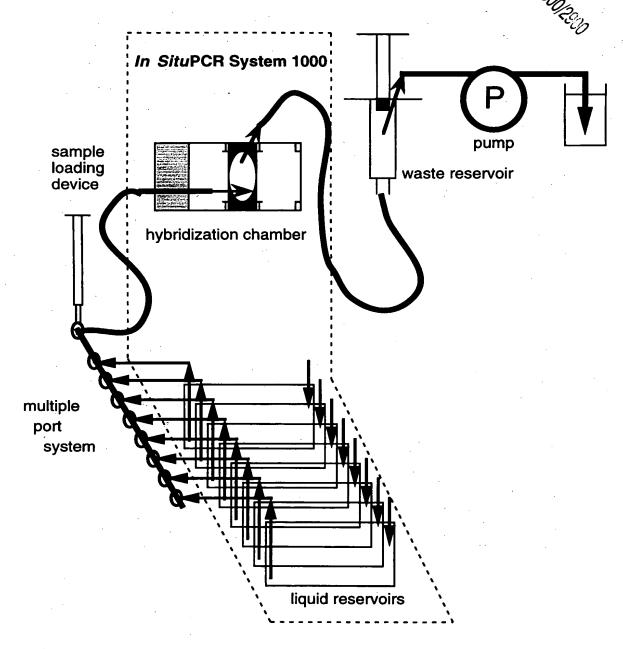


FIG. 27



TECHNIH BOOM

-C00H; PROBE 12

-COOH; PROBE 14

-NH2; PROBE 12

-NH2; PROBE 14



POLONIA POLOSON

2% EGDMA

2% HDDMA

4% EGDMA



1 0



FIG. 31

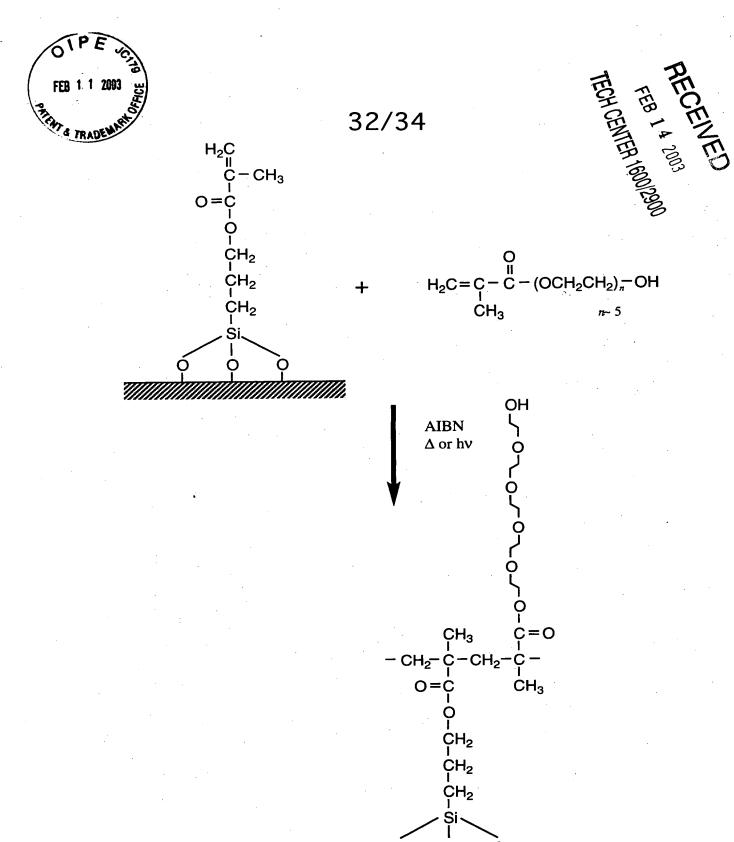


FIG. 32



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FIG. 33



FIG. 34